[11] JP 2001-164030
[43] Publication Date: June 19, 2001
[21] Japanese Patent Application No. Hei 11-352317
[22] Filing Date: December 10, 1999
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[54] Title of the Invention: POROUS MEMBRANE AND PRODUCTION PROCESS THEREOF

[TITLE OF THE INVENTION]

Porous Membrane and Production Process Thereof

[ABSTRACT]

[OBJECT] To provide a porous membrane useful in a test strip, which makes it possible to significantly shorten the time required for the spreading of a specimen such as blood and is adapted to measure a particular component in the specimen, such as blood sugar, with very high measurement accuracy.

[MEANS FOR THE ACHIEVEMENT OF THE OBJECT] An anisotropic porous membrane obtained by subjecting, to wet film-forming, a film-forming solution which contains a water-insoluble first component polymer as a film component and a water-soluble second component as an extractable component, the concentration of said first component polymer being from 12 to 15 wt%.

[Claims]

[Claim 1] An anisotropic porous membrane having an average pore size of from 0.1 to 2 μm, a membrane thickness of from 50 to 200 μm and a porosity of from 50 to 95%, a ratio of an average pore size in one of surfaces to an average pore size in the other surface being 1.5 or greater.

[Claim 2] An anisotropic porous membrane obtained by subjecting, to wet film-forming, a film-forming solution comprising a water-insoluble first component polymer as a film component and a water-soluble second component as an extractable component, a concentration of said first component polymer being from 12 to 15 wt%.

[Claim 3] The anisotropic porous membrane according to claim 2, wherein an average pore size is from 0.1 to 2 μm, a membrane thickness is from 50 to 200 μm and a porosity is from 50 to 95%, and a ratio of an average pore size in one of surfaces to an average pore size in the other surface is 1.5 or greater.

[Claim 4] The anisotropic porous membrane according to claim 2 or 3, wherein a charged ratio of said first component polymer to said second component in said film-forming solution is from 3:1 to 1.5:1.

[Claim 5] The anisotropic porous membrane according to

any one of claims 2 to 4, wherein said anisotropic porous membrane has been obtained by conducting wet film-forming in an aqueous solidifying medium which comprises from 60 to 80 w/w% of a solvent of said film-forming solution.

[Claim 6] The anisotropic porous membrane according to any one of claims 2 to 5, wherein said first component polymer is a polyethersulfone.

[Claim 7] The anisotropic porous membrane according to any one of claims 2 to 5, wherein said second component is polyvinylpyrrolidone.

[Claim 8] A test strip obtained by laminating, over a small average pore-size surface of the porous membrane according to any one of claims 1 to 7, another porous membrane.

[Claim 9] A process for producing an anisotropic porous membrane, which comprises subjecting, to wet film-forming, a film-forming solution comprising a water-insoluble first component polymer as a film component and a water-soluble second component as an extractable component, a concentration of said first component polymer being from 12 to 15 wt%.

[Claim 10] The process according to claim 9, wherein a film-forming solution comprising said first component polymer and said second component at a charged ratio of

from 3:1 to 1.5:1 is used.

[Claim 11] The process according to claim 9 or 10, wherein said wet film-forming is conducted in an aqueous solidifying medium which comprises from 60 to 80 w/w% of a solvent of said film-forming solution.

[Claim 12] The process according to any one of claims 9 to 11, wherein said first component polymer is a polyethersulfone.

[Claim 13] The process according to any one of claims 9 to 11, wherein said second component is polyvinylpyrrolidone.

[DETAILED DESCRIPTION OF THE INVENTION]

[0001]

[FIELD OF THE INVENTION] This invention relates to a porous membrane for measuring the amount of a target component in a specimen, for example, for measuring a blood sugar level, its production process, and a test strip making use of the porous membrane.

[0002]

[PRIOR ART] Blood sugar measuring instruments (blood component measuring instruments) are known to perform the measurement of blood sugar levels. These blood sugar measuring instruments each optically measures the degree of a color development on a test strip, which develops a

color in proportion to the level of glucose in blood, (performs a color measurement) to quantitate the blood sugar level. In such a conventional blood sugar measuring instrument, the measurement of a color on a test strip is performed by irradiating light onto the test strip in a light measuring unit, which is equipped with a light-emitting element and a light-receiving element, and measuring the intensity of light reflected from the test strip. Such a blood sugar measuring instrument, however, requires to perform operations such that, after blood (specimen) is supplied to a test paper and is allowed spread over the test strip, the test strip is inserted into a space maintained under light-shielded conditions and a measurement of blood sugar level is then started. Accordingly, the blood sugar measuring instrument is accompanied by a drawback that it is inferior in operability, and moreover, involves a potential problem in that the time from the supply of blood to the test strip until the measurement of its color may not be constant to develop a measurement error. There is, hence, an outstanding desire for the development of an automated blood sugar measuring instrument which permits a series of operations, ranging from the supply and spreading of a specimen to and over a test strip to its measurement, in

a continuous and automated manner.

[0003] Further, conventional test strips are each of the construction that a reagent is carried on a single sheet of base material composed of a porous material that can absorb a specimen. As the diameters of pores in the sheet of base material are as small as 0.5 μm or so, this test strip involves a problem in that its water permeability, in other words, its ability to permit spreading (of a specimen) is low and hence, the spreading of the specimen takes time. It is disadvantageous especially for the automated blood sugar measuring instrument that the time required for the spreading of a specimen is long as mentioned above.

[0004] As means for resolving such problems, Japanese Patent Laid-open No. Hei 11-183474 discloses: (1) a test strip composed of a first porous layer, which carries thereon a reagent that reacts with a particular component in a specimen to develop a color, and a second porous layer, which has a function to filter off solid matter in the specimen, stacked one over the other such that the test strip is used by supplying the specimen from the side of the first layer, (2) a test strip as described above under (1), in which both of the first layer and the second layer have hydrophilicity, (3) a test strip as

described above under (1) or (2), in which the diameters of pores in the first layer are from 8 to 50 μm, (4) a test strip as described above under any one of (1) to (3), in which the diameters of pores in the second layer are not greater than 5 μm, and (5) a test strip as described above under any one of (1) to (4), in which the specimen is blood and the solid matter is primarily composed of blood cells including red blood cells.

[0005] The use of a test strip composed of separate layers, a first layer and a second layer, as described above is described to resolve the above-mentioned problems. However, the use of such a test strip is accompanied by problems as will be described hereinafter. A porous membrane as the second layer is required to permit the prompt spreading of a plasma component, which has reacted with a reagent, over a measurement surface while filtering off blood cells. The smaller the pore size, the more effective for the filtering-off and elimination of blood cells. An excessively small pore size, however, leads to slower spreading of the plasma component. There is a method that makes the pore size large on an inlet side and small on an outlet side to eliminate blood cells while maintaining a spreading rate. When the elimination of blood cells is conducted

immediately upstream of a measurement surface, however, hemoglobin as a blood cell component is visible through the porous structure to affect the accuracy of the measurement.

[0006]

[OBJECTS TO BE ACHIEVED] Objects of the present invention are to provide a test strip for measuring a specific component in a specimen, which can significantly shorten the time required for the spreading of the specimen and has a very high measurement accuracy, a porous membrane useful in the test strip, and a production process of the porous membrane.

[0007]

[MEANS FOR ACHIEVING THE OBJECTS] These objects can be achieved by the present invention as will be described below.

(1) This invention provides an anisotropic porous membrane having an average pore size of from 0.1 to 2 μm, a membrane thickness of from 50 to 200 μm and a porosity of from 50 to 95%, a ratio of an average pore size in one of surfaces to an average pore size in the other surface being 1.5 or greater.

(2) This invention also provides an anisotropic porous membrane as described above under (1), which does not

permit permeation of red blood cells therethrough.

[0008] (3) This invention also provides an anisotropic porous membrane obtained by subjecting, to wet film-forming, a film-forming solution including a water-insoluble first component polymer as a film component and a water-soluble second component as an extractable component, a concentration of the first component polymer being from 12 to 15 wt%.

(4) This invention also provides an anisotropic porous membrane as described above under (3), wherein an average pore size is from 0.1 to 2 μm, a membrane thickness is from 50 to 200 μm and a porosity is from 50 to 95%, and a ratio of an average pore size in one of surfaces to an average pore size in the other surface is 1.5 or greater.

[0009] (5) This invention also provides an anisotropic porous membrane as described above under (3) or (4), which does not permit permeation of red blood cells therethrough.

(6) This invention further provides an anisotropic porous membrane as described above under any one of (3) to (5), wherein a charged ratio of the first component polymer to the second component in the film-forming solution is from 3:1 to 1.5:1.

[0010] (7) This invention further provides an anisotropic

porous membrane as described above under any one of (3) to (6), wherein the anisotropic porous membrane has been obtained by conducting wet film-forming in an aqueous solidifying medium which includes from 60 to 80 w/w% of a solvent of the film-forming solution.

(8) This invention further provides an anisotropic porous membrane as described above under any one of (3) to (7), wherein the first component polymer is a polyethersulfone.

[0011] (9) This invention further provides an anisotropic porous membrane as described above under any one of (3) to (7), wherein the second component is polyvinylpyrrolidone.

(10) This invention further provides a test strip obtained by laminating, over a small average pore-size surface of a porous membrane as described above under any one of (1) to (9), another porous membrane.

[0012] (11) This invention still further provides a process for producing an anisotropic porous membrane, which includes subjecting, to wet film-forming, a film-forming solution including a water-insoluble first component polymer as a film component and a water-soluble second component as an extractable component, a concentration of said first component polymer being from 12 to 15 wt%.

(12) This invention still further provides a process as described above under (11), wherein a film-forming solution including the first component polymer and the second component at a charged ratio of from 3:1 to 1.5:1 is used.

[0013] (13) This invention still further provides a process as described above under (11) or (12), wherein the wet film-forming is conducted in an aqueous solidifying medium which includes from 60 to 80 w/w% of a solvent of the film-forming solution.

(14) This invention still further provides a process as described above under any one of (11) to (13), wherein the first component polymer is a polyethersulfone.

(13) This invention still further provides a process as described above under any one of (11) to (13), wherein the second component is polyvinylpyrrolidone.

[0014]

[MODES FOR CARRYING OUT THE INVENTION] In the anisotropic porous membrane according to the present invention, the average pore size at one of its surfaces is smaller than the average particle size at the other surface. A specimen with a specific component contained therein is supplied from the one surface, and the measurement of the specific component is performed at the other surface by

an optical method. It is, therefore, considered necessary to filter off suspended matter such as blood cells and also to cause prompt spreading of the specific component such as a plasma component, which has reacted with a reagent, from the one surface to the other surface. The filtering off and elimination of suspended matter such as blood cells can be achieved by making the pore size smaller. However, an excessively small pore size leads to slow spreading of the specific component such as the plasma component. There is also a method that makes the pore size greater on a supplying side of the specific component such as a plasma component reacted with the reagent and smaller on the other side to eliminate suspended matter such as blood cells while maintaining a spreading rate. The filtering off and elimination of suspended matter is, however, conducted in the proximity of the measurement surface. Accordingly, hemoglobin as a blood cell component is visible through the porous structure to affect the accuracy of the measurement.

[0015] It is, therefore, possible to exactly perform the filtering off and elimination of suspended matter such as blood cells and also to improve the spreading rate of a specific component such as a plasma component to the surface on the measurement side and the accuracy of

measurement by forming an anisotropic structure that the surface pore size is made small on the side at which the specimen with the specific component contained therein is supplied and the surface pore size is made grater on the other side.

[0016] As a specific structure of the anisotropic porous membrane according to the present invention, the average pore size may be from 0.1 to 2 μm, desirably from 0.3 to 1.6 μm, more desirably from 0.5 to 1.3 μm. The ratio of the average pore size at the surface, at which the specific component in a specimen is measured, to the average pore size at the other surface may be 1.5 or greater, desirably 2.0 or greater, more desirably 2.3 or greater.

[0017] The thickness of the anisotropic porous membrane according to the present invention may be from 50 to 200 μm, desirably from 70 to 180 μm, more desirably from 80 to 150 μm, although no particular limitation is imposed thereon. This is because a membrane thickness smaller than 50 μm results in insufficient membrane strength, while a membrane thickness greater than 200 μm requires an excessively long time for the spreading of a specimen.

[0018] The porosity of the anisotropic porous membrane according to the present invention may be from 50 to 95%,

desirably from 70 to 90%, more desirably from 75 to 85%, although no particular limitation is imposed thereon. A porosity lower than 50% leads to a failure in absorbing and spreading a specimen in an amount as much as needed, while a porosity higher than 95% leads to insufficient membrane strength.

[0019] Examples of a polymer usable as a membrane material for the anisotropic porous membrane according to the present invention include nitrocellulose, polyvinyl difluoride, cellulose acetate, polysulfones, polyethersulfones, and polyethylene. Especially when a reagent is carried for use in measuring a blood sugar level, a polyethersulfone can be suitably used as the activity of the reagent is deteriorated least with time.

[0020] As a process for the production of the anisotropic porous membrane according to the present invention, wet film-forming is a desired process. As production processes of porous membranes, melt film-forming, dry film-forming and the like are also known. However, wet film-forming is a desired process when it is desired to produce an anisotropic membrane that the pore size of one surface is different from the pore size of the surface on the opposite side. The production process according to the present invention is carried out by spreading a film-

forming solution in the form of a film, conducting (its solidification) through an aqueous solidification medium, and then performing drying.

[0021] The step of spreading the film-forming solution in the form of the film can be conducted by ejecting, coating or otherwise applying the film-forming solution over a surface of a substrate such as glass plate. This method is effective for providing the final porous membrane with higher anisotropy and also for maintaining the ratio of the pore size of the one surface (which is kept in contact with air) to the pore size of the other surface (which is kept in contact with the substrate) at 1.5 or higher.

[0022] The film-forming solution for use in the present invention can desirably contain a water-insoluble first component polymer as a film component and a water-soluble second component as an extractable component, with the concentration of the first component polymer ranging from 12 to 15 wt%. The porous membrane according to the present invention has an average pore size of from 0.1 to 2 μm. Accordingly, a concentration of the first component higher than 15 wt% results in an excessively small pore size, while a concentration of the first component lower than 12 wt% leads to an excessively large

pore size. If produced from a single polymer solution of the first component polymer alone, the resulting membrane has a dense structure for the cohesion of the polymer. The addition of the water-soluble second component as an extractable component to the film-forming solution can inhibit the cohesion of the polymer, and can form pores in cavities left after the extraction and removal of the component and therefore, can increase the porosity.

[0023] Usable examples of the first component polymer include nitrocellulose, polyvinylidene fluoride, cellulose acetate, polysulfones, and polyethylene. Especially when a finally-obtained porous membrane is employed to carry a reagent for use in measuring a blood sugar level, a polyethersulfone can be suitably used as the activity of the reagent is deteriorated least with time. Examples of the water-soluble second component as an extractable component include polyvinylpyrrolidone, polyethylene glycol, polyacrylamide, polyacrylic acid, hydroxypropylcellulose, and methylcellulose, all of which are not soluble at all in the first component polymer but are soluble in a solvent and can be readily extracted out subsequent to solidification. Polyvinylpyrrolidone is particularly preferred owing to its properties that it is not soluble in nitrocellulose, polyvinyl difluoride,

cellulose acetate, polysulfones, polyethylene, polyethersulfones and the like but is soluble in a polar solvent which dissolves these polymers, and can be extracted out with water subsequent to solidification. Moreover, polyvinylpyrrolidone remains in a trace amount in the finally-obtained porous membrane even after its extraction, thereby also exhibiting an effect that owing to its compatibility with water, the porous membrane is assured to have hydrophilicity.

[0024] Examples of a solvent of the film-forming solution, which serves to dissolve the first component polymer and the water-soluble second component, include organic polar solvents, specifically N-methyl-2-pyrrolidone, dimethylformamide, dimethylsulfoxide, and dimethylacetamide. Particularly desired is N-methyl-2-pyrrolidone.

[0025] The charged ratio of the first component polymer to the second component in the film-forming solution may desirably be from 3:1 to 1.5:1. If the first component polymer is too much, the effect which is available from the addition of the second component, that is, the extractable component cannot be brought about so that large cavities are internally formed to fail at obtaining a stable porous structure. If the second component, that

is, the extractable component is too much, on the other hand, a dense structure is formed.

[0026] The aqueous solidification medium is an aqueous solidification medium containing 60 to 80 w/w%, desirably 65 to 75 w/w% of a solvent which is the same as the solvent of the film-forming solution. It is desired to conduct the solidification at a temperature of from 20 to 60°C, preferably from 25 to 50°C for a time of from 0.5 to 20 minutes, preferably from 1 to 10 minutes. If the solidification is conducted under completely solventless conditions, the film-forming solution spread in the form of a film rapidly solidifies at the surface thereof so that a dense layer called "a skin layer" is formed to fail at obtaining a porous structure as intended at the beginning. The solidification in the aqueous solidification medium, which contains 60 to 80 w/w% of a solvent which is the same as the solvent of the film-forming solution, makes it possible to realize slow solidification such that a porous structure is also formed at the surface. If the concentration of the solvent, which is the same as the solvent of the film-forming solution, in the solidification medium is lower than 60 w/w%, the above-mentioned effect available from its addition cannot be brought about. If the

concentration of the solvent in the solidification medium is higher than 80 w/w%, on the other hand, the solidification medium is not provided with sufficient solidifying ability.

[0027] A temperature lower than 20°C results in an excessively high deposition rate of the first component polymer, and hence, in a dense film. A temperature higher than 60°C results in an unduly slow deposition rate of the first polymer component so that no film is formed. A time shorter than 0.5 minute leads to absolutely no deposition of the first polymer component so that no film is formed, while a time longer than 20 minutes does not bring about any change to the film structure and leads to a reduction in production efficiency.

[0028] No particular limitation is imposed on the drying step. The drying step can be conducted, for example, by air drying or in an electric oven, at a temperature of from 25 to 100°C, desirably from 30 to 80°C for a time of from 1 to 24 hours, desirably from 4 to 18 hours.

[0029] Concerning the anisotropic porous membrane according to the present invention, it is desired for the prompt supply and spreading of a specimen to incorporate a hydrophilizing agent, to form the anisotropic porous membrane with a material having hydrophilicity, or to

apply hydrophilization processing. Examples of the hydrophilizing agent include surfactants such as "TRITON X-100", water-soluble silicones, hydroxypropylcellulose, polyethylene glycol, and polypropylene glycol. Examples of the hydrophilization processing include plasma processing, glow discharge, corona discharge, and ultraviolet exposure.

[0030] The anisotropic porous membrane according to the present invention is usable by itself. However, it is desired to use the anisotropic porous membrane as a test strip with another porous membrane laminated on the small average pore size surface of the first-mentioned membrane. It is to be noted that no particular limitation is imposed on the lamination method. For example, two membranes are simply stacked one over the other and are then united together along their circumferences, or two membranes are adhered with each other or are fusion-bonded together.

[0031] As the another porous membrane, one carrying a reagent that reacts with a specific component in a specimen to develop a color can be mentioned. It is to be noted that no particular limitation is imposed as to whether or not the porous membrane is anisotropic. Examples of the above-mentioned reagent which reacts with

the specific component in the specimen include enzyme preparations of glucose-oxidase (GOD)-like enzymes, peroxidase (POD)-like enzymes, ascorbate-oxidase-like enzymes, alcohol-oxidase-like enzymes, and cholesterol-oxidase-like enzymes; and color developers such as 4-aminoantipyrine and N-ethyl-N-(2-hydroxy-3-sulfopropyl)-m-toluidine. These reagents can be used either singly or in combination.

[0032] It is to be noted that the test strip according to the present invention is used by inserting it into a chip which can be detachably mounted on an instrument for measuring a particular component in a specimen or into a measuring instrument itself. Examples of the measuring instrument include instruments for quantitatively or qualitatively measuring the sugar, cholesterol, fat and the like in blood or the sugar, proteins, occult blood and the like in urine.

[0033]

[Examples] Specific examples of the present invention will hereinafter be described. Porous membranes of the individual examples and comparative examples were formed under the conditions to be described hereinafter. (In each of the examples and comparative examples), the film-forming solution shown in Table 1 was firstly supplied in

the form of a line on a substrate (glass plate) by a 50-mL syringe, and was then spread over the glass plate by an applicator with a 125-μm gap. The glass plate with the film-forming solution spread thereon was immersed in a solidification medium composed of an aqueous solution of N-methyl-2-pyrrolidone (NMP) prepared at the solvent concentration shown in Table 1, and the first component polymer was caused to deposit. The temperature of the solidification medium was set at 35°C. Subsequently, the solvent component and the water-soluble second component were extracted out in a water bath, followed by drying in an oven at 40°C to obtain a test strip. Employed were a polyethersulfone ("SUMIKAEXEL 7300P", product of Sumitomo Chemical Co., Ltd.) as the first component polymer, polyvinylpyrrolidone ("BASF POLYVINYLPYRROLIDONE K-90", product of BASF AG) as a second component, and N-methyl-2-pyrrolidone (product of BASF AG) as a solvent.

[0034] The average pore sizes of the membranes formed as described above are shown in Table 2. The average pore size of the membrane of each example was measured by capillary flow porometry in accordance with ASTM F316-86. As a measuring instrument, "PALM POROSIMETER" (manufactured by Porous Material Inc.) was used. Concerning the average surface pore size of the membrane

of each example, an image taken by a scanning electron microscope ("JSM-840", manufactured by JEOL, Ltd.) was analyzed by an image analyzer ("IP-1000PC", manufactured by Asahi Kasei Corporation) such that the diameters of pores in a field of vision were calculated as circle equivalent diameters in terms of area and their mean was recorded as the average surface pore size. Therefore, a correlation is not necessarily established between the average pore size and average surface pore size of each membrane. The thickness of each membrane was measured by a micrometer (manufactured by Mitsutoyo Corporation). Each porosity was measured by the weight method.

[0035]

[Table 1]

Table 1 Film-forming conditions

	Concentration of the first component polymer (wt%)	Charged ratio of the first component/the second component	Concentration of solvent in solidification medium (w/w%)
Comp. Ex. 1	11	2/1	70
Ex. 1	12	2/1	70
Ex. 2	13	2/1	70
Ex. 3	14	2/1	70
Ex. 4	15	2/1	70
Comp. Ex. 2	16	2/1	70
Comp. Ex. 3	13	1/1	70
Ex. 5	13	1.5/1	70
Ex. 3	13	2/1	70
Ex. 6	13	3/1	70
Comp. Ex. 4	13	4/1	70
Comp. Ex. 5	13	2/1	50
Ex. 7	13	2/1	60
Ex. 3	13	2/1	70
Ex. 8	13	2/1	80
Comp. Ex. 6	13	2/1	90

[0036]

[Table 2]

Table 2 Measurement Results of Physical Properties

Average pore size (μm)		Average surface pore size				
		Open-side, small pore-size surface	Substrate-side, large pore-size surface	Ratio of large pore size/small pore size	Membrane thickness, μm	Porosity, %
Comp. Ex. 1	3.14	0.2	2.4	12.0	90	82
Ex. 1	1.89	0.2	1.9	9.5	97	82
Ex. 2	0.86	0.2	2.0	10.0	105	81
Ex. 3	0.48	0.2	1.4	7.0	106	81
Ex. 4	0.11	0.1	0.3	3.0	105	80
Comp. Ex. 2	0.06	0.1	0.2	2.0	108	78
Comp. Ex. 3	4.01	0.2	4.7	23.5	109	83
Ex. 5	1.77	0.2	1.9	9.5	106	82
Ex. 3	0.86	0.2	2.0	10.0	105	81
Ex. 6	0.29	0.2	1.1	5.5	102	80
Comp. Ex. 4	0.07	0.1	0.2	2.0	99	78
Comp. Ex. 5	Unable to measure	0.01	0.03	3.0	110	67
Ex. 7	0.34	0.2	1.3	6.5	108	78
Ex. 3	0.86	0.2	2.0	10.0	105	81
Ex. 8	1.31	0.2	1.9	9.5	101	83
Comp. Ex. 6	MI1	←	←	←	←	←

MI1: Measurement Impossible 1 - Measurements were impossible as the dope did not solidify.

[0037] (Test 1) Using the porous membranes of the above examples and comparative examples, the following experiment was conducted. Each membrane to be evaluated was coated with a coating reagent system to be described subsequently herein. The membrane to be evaluated was fixed on a sample holder of a spectrophotometer ("UV-2400(PC)S", manufactured by Shimadzu Corporation) to permit the measurement of its reflection absorbance. Human blood (5 μL) was added to a small pore-size surface by a micropipette (manufactured by Eppendorf AG), and changes in reflection absorbance on the opposite surface were measured with time. The period from a time point at which the rate of a change per second in reflectance exceeded 1% until a time point at which the rate of a change per second in reflectance fell short of 1% was used as Δt. The results are shown in Table 3.

[0038] Coating reagent system: GOD, POD, and 4-aminoantipyrine, N-ethyl-N-(2-hydroxy-3-sulfopropyl)-m-toluidine (TOOS), "Triton X-100".

[0039] Measurement conditions

Changes with time

Measurement value: reflectance

Wavelength: 610 nm

Slit width: 2.0 nm

Timing mode: auto

Measurement time: 90 sec

Sampling pitch: 0.1 sec

Cell number: 1

Data number: 901

[0040] (Test 2) Using the porous membranes of the above examples and comparative examples, the following experiment was conducted. Each membrane to be evaluated was coated with the above-described coating reagent system. The membrane to be evaluated was fixed on a sample holder of a spectrophotometer ("UV-2400(PC)S", manufactured by Shimadzu Corporation) to permit the measurement of its reflection absorbance. Human blood (5 μL) was added to an inlet-side surface by a micropipette (manufactured by Eppendorf AG), and a reflective absorption spectrum of reflection absorbance on the opposite surface was measured. It is to be noted that the addition of the blood was conducted from the small pore-size surface. Compared with a spectrum measured when plasma was added, it was determined whether or not the measurement was affected by hemoglobin. The results are shown in Table 3.

[0041] Measurement conditions

Reflective absorption spectrum

Measurement value: reflectance

Wavelength range (nm): 700 (start) 500 (end)

Scanning speed: medium

Slit width: 2.0 nm

Sampling pitch: 1.0 nm

[0042]

[Table 3]

	Test 1 Soak-through time (sec)	Test 2 Effect of hemoglobin
Comp. Ex. 1	4.6	Affected
Ex. 1	5.2	Not affected
Ex. 2	5.7	Not affected
Ex. 3	6.8	Not affected
Ex. 4	7.3	Not affected
Comp. Ex. 2	10.9	Not affected
Comp. Ex. 3	4.1	Affected
Ex. 5	5.5	Not affected
Ex. 3	5.7	Not affected
Ex. 6	7.0	Not affected
Comp. Ex. 4	10.2	Not affected
Comp. Ex. 5	No soak through	-
Ex. 7	7.1	Not affected
Ex. 3	5.7	Not affected
Ex. 8	5.4	Not affected
Comp. Ex. 6	-	-

[0043]

[EFFECTS OF THE INVENTION] The porous membrane according to the present invention is fast in the spreading rate of a specimen and can shorten the time required for

spreading, and upon colorimetric measurement, can filter off suspended matter in the specimen and permits a measurement with higher accuracy. The porous membrane according to the present invention, when stacked with another porous membrane, can provide a test strip for the measurement of a specific component in a specimen, which can significantly shorten the time required for the spreading of the specimen and is very high in the accuracy of measurement.

[0044] In particular, the porous membrane according to the present invention is effectively usable in a blood sugar test strip which is adapted to measure the sugar level in blood. It is high in the spreading rate of the blood and can shorten the time required for the spreading, and can sufficiently filter off solid matter such as red blood cells to eliminate the effect of hemoglobin such as red blood cells, thereby allowing to conduct the measurement with higher accuracy.

[0045] The production process according to the present invention can produce a porous membrane, which is high in the spreading rate of a specimen and can shorten the time required for its spreading, and upon colorimetric measurement, can filter off suspended matter in the specimen, thereby allowing to conduct the measurement

with higher accuracy. The porous membrane obtained by the production process of the present invention, when stacked with another porous membrane, can provide a test strip for the measurement of a specific component in a specimen, which can significantly shorten the time required for the spreading of the specimen and is very high in the accuracy of measurement.

[0046] In particular, the porous membrane obtained by the production process of the present invention is effectively usable in a blood sugar test strip which is adapted to measure the sugar level in blood. It is high in the spreading rate of the blood and can shorten the time required for the spreading, and can sufficiently filter off solid matter such as red blood cells to eliminate the effect of hemoglobin such as red blood cells, thereby allowing to conduct the measurement with higher accuracy.

(19)日本国特許庁（ＪＰ）　(12)公開特許公報（Ａ）　(11)特許出願公開番号
特開2001－164030
（P2001－164030A）
(43)公開日　平成13年６月19日(2001.6.19)

(51)Int.Cl.'	識別記号	FI		テーマコード'(参考)
C08J 9/26		C08J 9/26		2G042
G01N 31/22	121	G01N 31/22	121P	2G045
33/52		33/52	B	4F074
// C08L 81/06		C08L 81/06		4J002

審査請求　未請求　請求項の数13　ＯＬ　（全 7 頁）

(21)出願番号　特願平11－352317

(22)出願日　平成11年12月10日(1999.12.10)

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(54)【発明の名称】　多孔質膜およびその製造方法

(57)【要約】
【課題】血液などの検体の展開に要する時間を飛躍的に短縮することができ、かつ非常に測定精度が高い、血糖などの検体中の特定成分を測定する試験紙に使用する多孔質膜を提供する。
【解決手段】膜成分となる非水溶性第１成分ポリマーと被抽出成分である水溶性第２成分を含み、第１成分ポリマーの濃度が１２～１５ｗｔ％の製膜原液を湿式製膜することによって得られる異方性の多孔質膜。

【特許請求の範囲】
【請求項１】平均孔径が０．１～２μm、膜厚が５０～２００μm及び空孔率が５０～９５％の多孔質膜であり、一方の表面の平均孔径と他方の表面の平均孔径の比が１．５以上である異方性の多孔質膜。
【請求項２】膜成分となる非水溶性第１成分ポリマーと被抽出成分である水溶性第２成分を含み、第１成分ポリマーの濃度が１２～１５ｗｔ％の製膜原液を湿式製膜することによって得られる異方性の多孔質膜。
【請求項３】平均孔径が０．１～２μm、膜厚が５０～２００μm及び空孔率が５０～９５％の多孔質膜であり、一方の表面の平均孔径と他方の表面の平均孔径の比が１．５以上である請求項２に記載の異方性の多孔質膜。
【請求項４】前記製膜原液の前記第１成分ポリマーと前記第２成分との仕込み比が３：１～１．５：１である請求項２乃至３に記載の異方性の多孔質膜。
【請求項５】６０～８０w/w％の前記製膜原液の溶媒を含む水系凝固浴を行い湿式製膜することによって得られる請求項２乃至４に記載の異方性の多孔質膜。
【請求項６】前記第１成分ポリマーがポリエーテルスルホンである請求項２乃至５に記載の異方性の多孔質膜。
【請求項７】前記第２成分がポリビニルピロリドンである請求項２乃至５に記載の異方性の多孔質膜。
【請求項８】請求項１乃至７に記載の多孔質膜の平均孔径の小さい面に、他の多孔質膜を積層することによって得られる試験紙。
【請求項９】膜成分となる非水溶性第１成分ポリマーと被抽出成分である水溶性第２成分を含み、第１成分ポリマーの濃度が１２～１５ｗｔ％の製膜原液を用いて湿式製膜することを特徴とする異方性の多孔質膜の製造方法。
【請求項１０】前記第１成分ポリマーと前記第２成分との仕込み比が３：１～１．５：１の製膜原液を用いることを特徴とする請求項９に記載の異方性の多孔質膜の製造方法。
【請求項１１】６０～８０w/w％の前記製膜原液の溶媒を含む水系凝固浴を行い湿式製膜することを特徴とする請求項９乃至１０に記載の異方性の多孔質膜の製造方法。
【請求項１２】前記第１成分ポリマーがポリエーテルスルホンであることを特徴とするを特徴とする請求項９乃至１１に記載の異方性の多孔質膜の製造方法。
【請求項１３】前記第２成分がポリビニルピロリドンであることを特徴とする請求項９乃至１１に記載の異方性の多孔質膜の製造方法。
【発明の詳細な説明】
【０００１】
【発明が属する技術分野】本発明は、例えば血糖値の測定のような、検体中の目的成分の量を測定する多孔質膜、その製造方法、及びその多孔質膜を用いた試験紙に関するものである。
【０００２】
【従来の技術】血糖値の測定を行う血糖測定装置（血中成分測定装置）が知られている。この血糖測定装置は、血中のブドウ糖量に応じて呈色する試験紙の呈色の度合いを光学的に測定（測色）して血糖値を定量化するものである。このような従来の血糖測定装置では、試験紙の測色は、発光素子および受光素子を備える測光部において、試験紙に光を照射しその反射光の強度を測定することにより行われている。この血糖測定装置では、試験紙に血液（検体）を供給・展開する操作を行った後、その試験紙を遮光状態が確保される空間へ挿入し、血糖値の測定を開始するが、操作性が劣るという欠点があるとともに、試験紙への血液の供給から測色までの時間が一定でなく、それによる測定誤差が生じるという問題がある。そのため、試験紙への供給・展開から測定までの一連の操作を連続的、自動的に行うことが出来る血糖自動測定装置の開発が望まれている。
【０００３】また、従来の試験紙は、検体を吸収可能な多孔質材料で構成された１枚のシート基材に試薬を担持させた構成のものである。この試験紙では、シート基材の細孔の孔径が０．５μm程度と小さいため、通水性、すなわち展延性が低く、そのため検体の展開に時間がかかるという問題がある。このように検体の展開に要する時間が長いということは、とくに、前記血糖自動測定装置にとって不利である。
【０００４】また、このような問題点を解決する手段として、（１）検体中の特定成分と反応して呈色する試薬を担持する多孔質の第１の層と、検体中の濾別物を濾別する機能を有する多孔質の第２の層とを積層してなり、前記第１の層側から検体を供給して使用することを特徴とする試験紙、（２）前記第１の層および前記第２の層がそれぞれ親水性を有している上記（１）に記載の試験紙、（３）前記第１の層における細孔の孔径が８～５０μmである上記（１）または（２）に記載の試験紙、（４）前記第２の層における細孔の孔径が５μm 以下である上記（１）ないし（３）のいずれかに記載の試験紙、及び（５）前記検体は血液であり、前記濾別物は主に赤血球を含む血球である上記（１）ないし（４）のいずれかに記載の試験紙が、特開平１１－１８３４７４号で示されている。
【０００５】以上のような第１の層と第２の層に分かれた試験紙を使用することで、前述の問題が解決されるという。しかしながらこのような試験紙を用いた場合にも、以下のような問題点がある。第２層目の多孔質膜は、血球を濾別しつつ試薬と反応した血漿成分を迅速に測定面へ展開させうることが要求される。血球を濾別・除去するためには孔径を小さくする程効果があるが、孔径を小さくしすぎると血漿成分の展開が遅くなる。ま

た、入り口側の孔径を大きくし、出口側の孔径を小さくすることで展開速度を維持しつつ血球を除去する方法もあるが、血球除去が測定面直前で行われたのでは、血球成分の血色素が多孔質構造を通して透けて見えてしまい、測定精度に影響してしまう。

【０００６】

【発明が解決しようとする課題】本発明の目的は、検体の展開に要する時間を飛躍的に短縮することができ、かつ非常に測定精度が高い、検体中の特定成分測定用試験紙、それに用いる多孔質膜、及び多孔質膜の製造方法を提供することにある。

【０００７】

【課題を解決するための手段】このような目的は、下記の本発明により達成される。

（１）本発明は、平均孔径が０．１～２μｍ、膜厚が５０～２００μｍ及び空孔率が５０～９５％の多孔質膜であり、一方の表面の平均孔径と他方の表面の平均孔径の比が１．５以上である異方性の多孔質膜である。

（２）本発明は、赤血球が透過しない上記（１）に記載の異方性の多孔質膜である。

【０００８】（３）本発明は、膜成分となる非水溶性第１成分ポリマーと被抽出成分である水溶性第２成分を含み、第１成分ポリマーの濃度が１２～１５ｗｔ％の製膜原液を湿式製膜することによって得られる異方性の多孔質膜である。

（４）本発明は、平均孔径が０．１～２μｍ、膜厚が５０～２００μｍ及び空孔率が５０～９５％の多孔質膜であり、一方の表面の平均孔径と他方の表面の平均孔径の比が１．５以上である上記（３）に記載の異方性の多孔質膜である。

【０００９】（５）本発明は、赤血球が透過しない上記（３）乃至（４）に記載の異方性の多孔質膜である。

（６）本発明は、前記製膜原液の前記第１成分ポリマーと前記第２成分との仕込み比が３：１～１．５：１である上記（３）乃至（５）に記載の異方性の多孔質膜である。

【００１０】（７）本発明は、６０～８０w/w％の前記製膜原液の溶媒を含む水系凝固浴を行い湿式製膜することによって得られる上記（３）乃至（６）に記載の異方性の多孔質膜である。

（８）本発明は、前記第１成分ポリマーがポリエーテルスルホンである上記（３）乃至（７）に記載の異方性の多孔質膜である。

【００１１】（９）本発明は、前記第２成分がポリビニルピロリドンである上記（３）乃至（７）に記載の異方性の多孔質膜である。

（１０）本発明は、上記（１）乃至（９）に記載の多孔質膜の平均孔径の小さい面に、他の多孔質膜を積層することによって得られる試験紙である。

【００１２】（１１）本発明は、膜成分となる非水溶性第１成分ポリマーと被抽出成分である水溶性第２成分を含み、第１成分ポリマーの濃度が１２～１５ｗｔ％の製膜原液を用いて湿式製膜することを特徴とする異方性の多孔質膜の製造方法である。

（１２）本発明は、前記第１成分ポリマーと前記第２成分との仕込み比が３：１～１．５：１の製膜原液を用いることを特徴とする上記（１１）に記載の異方性の多孔質膜の製造方法である。

【００１３】（１３）本発明は、６０～８０w/w％の前記製膜原液の溶媒を含む水系凝固浴を行い湿式製膜することを特徴とする上記（１１）乃至（１２）に記載の異方性の多孔質膜の製造方法である。

（１４）本発明は、前記第１成分ポリマーがポリエーテルスルホンであることを特徴とするを特徴とする上記（１１）乃至（１３）に記載の異方性の多孔質膜の製造方法である。

（１３）本発明は、前記第２成分がポリビニルピロリドンであることを特徴とする上記（１１）乃至（１３）に記載の異方性の多孔質膜の製造方法である。

【００１４】

【発明の実施の形態】本発明の異方性の多孔質膜は、一方の表面の平均孔径が他方の表面の平均孔径よりも小さいものであり、一方の表面から特定成分を含む検体を供給し、他方の表面から光学的方法などにより特定成分の測定を行うものである。そのため、血球などの浮遊物を濾別し、試薬と反応した血漿成分などの特定成分を迅速に一方の表面から他方の表面へ展開させることが必要とされる。血球などの浮遊物を濾別・除去するためには、孔径を小さくすることで解決できるが、孔径を小さくしすぎると血漿成分などの特定成分の展開が遅くなってしまう。また、試薬と反応した血漿成分などの特定成分を供給する側の孔径を大きくし、他方の孔径を小さくすることで展開速度を維持しつつ血球などの浮遊物を除去する方法もあるが、浮遊物の濾別・除去が測定する表面の近くで行われるため、血球成分の血色素が多孔質構造を通して透けて見えてしまい測定の精度に影響を及ぼしてしまう。

【００１５】そこで、特定成分を含む検体供給する側の表面の孔径を小さくし、他方の孔径を大きくする異方性構造とすることで、血球などの浮遊物を濾別・除去を的確に行うとともに、血漿成分などの特定成分の測定する側の表面への展開速度、測定精度を向上させることが可能となる。

【００１６】本発明の異方性の多孔質膜の具体的な構造として、平均孔径は０．１～２μｍ、望ましくは０．３～１．６μｍ、より望ましくは０．５～１．３μｍであり、検体中の特定成分を測定する側の表面の平均孔径と他方の表面の平均孔径との比は１．５以上、望ましくは２．０以上、より望ましくは２．３以上である。

【００１７】本発明の異方性の多孔質膜の膜厚は、特に

限定しないが５０～２００μｍ、望ましくは７０～１８０μｍ、より望ましくは８０～１５０μｍである。膜厚が５０μｍを下回ると、膜強度が不足してしまい、２００μｍを越えてしまうと検体の展開に時間がかかってしまうためである。

【００１８】本発明の異方性の多孔質膜の空孔率は、特に限定しないが５０～９５%、望ましくは７０～９０%、より望ましくは７５～８５%である。空孔率が５０%を下回ると必要な量の検体を吸収展開することが出来なくなり、９５%を越えると膜強度が不足してしまうためである。

【００１９】本発明の異方性の多孔質膜の膜材質となるポリマーとしては、ニトロセルロース、ポリビニルジフロライド、セルロースアセテート、ポリスルホン、ポリエーテルスルホン、ポリエチレンなどが使用できるが、とりわけ血糖値を測定するために使用する試薬を担持した場合には、ポリエーテルスルホンが試薬活性の経時的劣化が最も少なく好適に使用できる。

【００２０】本発明の異方性の多孔質膜の製造方法としては、湿式製膜が望ましい方法である。多孔質膜の製造方法としては、他にも溶融製膜、乾式製膜なども知られているが、一方の表面の孔径が反対側の表面の孔径と異なる異方性膜を製造するには湿式製膜が望ましい方法である。本発明の製造方法は、製膜原液を膜状に広げ水系凝固浴を行い乾燥させることによって行われる。

【００２１】製膜原液を膜状に広げる工程は、ガラスなどの基材の表面に製膜原液を押し広げあるいは塗り広げることなどにより行われる。この方法は、最終的に得られる多孔質膜の異方性を高め、多孔質膜の一方の表面（空気に接する面）の孔径と他方の表面（基材に接する面）の孔径の比を１．５以上に保つのに有効である。

【００２２】本発明に用いる製膜原液は、膜成分となる非水溶性第１成分ポリマーと被抽出成分である水溶性第２成分を含み、第１成分ポリマーの濃度が１２～１５ｗｔ%のものが望ましい。本発明の多孔質膜は、平均孔径が０．１～２μｍの範囲が好適である。そのため第１成分ポリマー濃度が１５ｗｔ%を越えてしまっては孔径が小さくなってしまい、１２ｗｔ%を下回ったのでは孔径が大きくなりすぎてしまう。また、第１成分ポリマーのみの単一のポリマー溶液から製造した場合、そのポリマーの凝集力により緻密な構造となってしまうが、被抽出成分である水溶性第２成分を製膜原液に添加することで、ポリマーの凝集を抑制し、また該成分を抽出除去したあとの空間に孔が形成され空孔率を向上させることが出来る。

【００２３】第１成分ポリマーとしては、ニトロセルロース、ポリフッ化ビニリデン、セルロースアセテート、ポリスルホン、ポリエチレンなどが使用できるが、最終的に得られる多孔質膜がとりわけ血糖値を測定するために使用する試薬を担持する場合には、ポリエーテルスルホンが試薬の経時劣化が最も少なく好適に使用できる。被抽出成分である水溶性第２成分としては、第１成分ポリマーと完全に溶解せず、溶媒には溶解し、凝固後に容易に抽出除去できるポリビニルピロリドン、ポリエチレングリコール、ポリアクリルアミド、ポリアクリル酸、ヒドロキシプロピルセルロース、メチルセルロースなどがあげられる。特にポリビニルピロリドンはニトロセルロース、ポリビニルジフロライド、セルロースアセテート、ポリスルホン、ポリエチレン、ポリエーテルスルホンなどとは溶解せず、これらのポリマーを溶かす極性溶媒に溶解し、凝固後には水により抽出除去できるといった特性を持つため望ましい。さらに、ポリビニルピロリドンは抽出後も微量であるが最終的に得られる多孔質膜に残存し、その水親和性から多孔質膜の親水性を確保する効果も有する。

【００２４】第１成分ポリマーと水溶性第２成分の溶解を目的とする製膜原液の溶媒としては、具体的には、Ｎ－メチル－２－ピロリドン、ジメチルホルムアミド、ジメチルスルホキシド、ジメチルアセトアミドなどの有機極性溶媒などがあげられるが、特に望ましいのはＮ－メチル－２－ピロリドンである。

【００２５】製膜原液の第１成分ポリマーと被抽出成分である水溶性第２成分との仕込み比は、３：１～１．５：１であることが望ましい。第１成分ポリマーが多すぎると第２成分の被抽出成分の添加効果が得られずに、内部に大きな空孔が形成され、安定した多孔質構造が得られなくなり、第２成分の被抽出成分が多すぎると緻密な構造となるためである。

【００２６】水系凝固浴は、６０～８０w/w%、望ましくは６５～７５w/w%の上記製膜原液の溶媒を含む水系凝固浴で、温度が２０～６０℃、望ましくは２５～５０℃、時間が０．５～２０分間、望ましくは１～１０分間の条件で行うことが望ましい。凝固浴を１００%非溶媒で行うと、膜状に広げられた製膜原液がその表面において急速に凝固するため緻密なスキン層と呼ばれる層が形成されてしまい、当初の目的の多孔質構造が得られない。そのため、６０～８０w/w%の上記製膜原液の溶媒を含む水系凝固浴を行うことで、緩慢な凝固が実現し、表面にも多孔質構造が形成される。凝固浴中の製膜原液の溶媒の濃度が６０w/w%を下回ると上述した製膜原液の溶媒の添加効果が得られず、８０w/w%を越えると凝固能が不足してしまう。

【００２７】温度が２０℃を下回ると第１成分ポリマーの析出速度が速すぎて緻密な膜になってしまう。温度が６０℃を上回ると第１成分ポリマーの析出速度が遅すぎて膜が形成されない。また、時間が０．５分より短いと第１成分ポリマーが全て析出しないため膜が形成されず、時間が２０分より長いと膜構造は変化せず生産効率が低下してしまう。

【００２８】乾燥工程は、特に限定されず、例えば自然

乾燥や電気オーブンなどで、温度が２５～１００℃、望ましくは３０～８０℃、時間が１～２４時間、望ましくは４～１８時間の条件で行う方法などがあげられる。

【００２９】本発明の異方性の多孔質膜は、検体の供給、展開を迅速に行うため、親水化剤を含ませる、親水性を有する材質から構成する、あるいは親水化処理を行うことが望ましい。親水化剤としては、トライトンＸ－１００などの界面活性剤、水溶性シリコン、ヒドロキシプロピルセルロース、ポリエチレングリコール、ポリプロピレングリコールなどがあげられる。親水化処理としては、プラズマ処理、グロー放電、コロナ放電、紫外線照射などの処理方法があげられる。

【００３０】本発明の異方性の多孔質膜は単独での使用も可能だが、本多孔質膜の平均孔径の小さい面に、他の多孔質膜を積層することによって得られる試験紙として使用することが望ましい。なお、積層方法は特に限定することなく、例えば、単に重ね合わせ周囲を固定する方法、接着・融着する方法などがあげられる。

【００３１】他の多孔質膜としては、検体中の特定成分と反応して呈色する試薬を担持するものがあげられる。なお、当該多孔質膜が異方性であるか否かは特に限定されない。上述した検体中の特定成分と反応する試薬としては、グルコースオキシターゼ（ＧＯＤ）様酵素、ペルオキシターゼ（ＰＯＤ）様酵素、アスコルビン酸オキシダーゼ様酵素、アルコールオキシダーゼ様酵素、及びコレステロールオキシダーゼ様酵素などの酵素剤、及び４－アミノアンチピリン、Ｎ－エチル－Ｎ－（２－ヒドロキシ－３－スルホプロピル）－ｍ－トルイジンなどの発色剤があげられ、これらの単数あるいは複数を使用することができる。

【００３２】なお、本発明の試験紙は、検体中の特定成分の測定装置に脱着可能なチップ、あるいは測定装置自体に挿入して使用させるものである。測定装置とは、血液中の糖分、コレステロールや中性脂肪などや、尿中の糖分、蛋白や潜血などを、定量的あるいは定性的に測定する装置があげられる。

【００３３】

【実施例】以下、本発明の具体的実施例について説明する。各実施例及び比較例の多孔質膜を、以下に示す条件で製膜した。まず、表１に示す製膜原液を基材（ガラス板）上に５０ｍｌシリンジにて線状に供給し、これをギャップ１２５μｍのアプリケーターによりガラス板上に塗り拡げた。これを、表１に示す溶媒濃度で調製されたＮ－メチル－２－ピロリドン（ＮＭＰ）水溶液からなる凝固浴中に浸漬し、第１成分ポリマーを析出させた。凝固浴の温度は３５℃とした。その後、水浴中で溶剤成分、水溶性第２成分を抽出除去した後、４０℃オーブン中で乾燥させて試験紙を得た。第１成分ポリマーとしてポリエーテルスルホン（スミカエクセル７３００Ｐ、住友化学(株)製）を、第２成分としてポリビニルピロリドン（ＢＡＳＦポビドンＫ－９０、ＢＡＳＦ製）を、溶媒としてＮ－メチル－２－ピロリドン（ＢＡＳＦ製）を用いた。

【００３４】表２に製膜された各膜の平均孔径を示す。各例の膜の平均孔径はＡＳＴＭ　Ｆ３１６－８６に従いキャピラリィ フロー ポロメトリィ（Capillary Flow Porometry）によって測定した。測定装置はパームポロシメーター（ＰＭＩ社製）を使用した。各例の膜の表面平均孔径は走査型電子顕微鏡（ＪＳＭ－８４０日本電子製）で撮影した画像を画像解析装置（ＩＰ－１０００ＰＣ　旭化成製）により解析し、視野内の孔の孔径を面積換算で円相当径として算出し、相加平均を表面平均孔径とした。したがって、膜の平均孔径と、表面平均孔径は必ずしも相関関係が成り立つわけではない。膜厚はマイクロメーター（ミツトヨ精機製）にて測定した。空孔率は重量法にて測定した。

【００３５】

【表１】

【表１】表１　製膜条件

	第１成分ポリマー濃度（wt%）	第１成分／第２成分 仕込み比	凝固浴中溶媒濃度（w/w%）
比較例１	１１	２／１	７０
実施例１	１２	２／１	７０
実施例２	１３	２／１	７０
実施例３	１４	２／１	７０
実施例４	１５	２／１	７０
比較例２	１６	２／１	７０
比較例３	１３	１／１	７０
実施例５	１３	１．５／１	７０
実施例３	１３	２／１	７０
実施例６	１３	３／１	７０
比較例４	１３	４／１	７０
比較例５	１３	２／１	５０
実施例７	１３	２／１	６０
実施例３	１３	２／１	７０
実施例８	１３	２／１	８０
比較例６	１３	２／１	９０

【００３６】

【表２】

【表２】

表２　物性測定結果

	平均孔径（μm）	表面平均孔径				
		開放面孔径小面	基材側面孔径大面	孔径大/小比	膜厚 μm	空孔率 %
比較例１	３．１４	０．２	２．４	１２．０	９０	８２
実施例１	１．８９	０．２	１．９	９．５	９７	８２
実施例２	０．８６	０．２	２．０	１０．０	１０５	８１
実施例３	０．４８	０．２	１．４	７．０	１０６	８１
実施例４	０．１１	０．１	０．３	３．０	１０５	８０
比較例２	０．０６	０．１	０．２	２．０	１０８	７８
比較例３	４．０１	０．２	４．７	２３．５	１０９	８３
実施例５	１．７７	０．２	１．９	９．５	１０６	８２
実施例３	０．８６	０．２	２．０	１０．０	１０５	８１
実施例６	０．２９	０．２	１．１	５．５	１０２	８０
比較例４	０．０７	０．１	０．２	２．０	９９	７８
比較例５	測定できず	０．０１	０．０３	３．０	１１０	６７
実施例７	０．３４	０．２	１．３	６．５	１０８	７８
実施例３	０．８６	０．２	２．０	１０．０	１０５	８１
実施例８	１．３１	０．２	１．９	９．５	１０１	８３
比較例６	測定不能１	←	←	←	←	←

測定不能１；ドープが凝固しないため測定不能

【００３７】（試験例１）上記の各実施例および比較例の多孔質膜を用い、次の実験を行った。評価する膜に下に示すコート試薬をコートした。評価する膜を反射吸光度が測定できるように分光光度計（ＵＶ－２４００（ＰＣ）Ｓ　島津製作所社製）のサンプルホルダーに固定し、ヒト血液を孔径の小さい面へマイクロピペット（エッペンドルフ社製）で５μｌ添加し、反対面の反射吸光度の時間変化を測定した。１秒間の反射率の変化割合が、１％を超えた時から、１秒間の反射率の変化割合が１％を下回ったときまでの時間をΔｔとした。結果を表３に示す。

【００３８】コート試薬：ＧＯＤ、ＰＯＤおよび４－アミノアンチピリン、Ｎ－エチル－Ｎ－（２－ヒドロキシ－３－スルホプロピル）－ｍ－トルイジン（ＴＯＯＳ）、トライトンＸ－１００

【００３９】測定条件

時間変化

測光値：反射率

波長：６１０ｎｍ

スリット幅：２．０ｎｍ

タイミングモード：オート

測定時間：９０秒

サンプリングピッチ：０．１sec

セル数：１

データ数：９０１

【００４０】（試験例２）上記の各実施例および比較例の多孔質膜を用い、次の実験を行った。評価する膜に上に示すコート試薬をコートした。評価する膜を反射吸光度が測定できるように分光光度計（ＵＶ－２４００（ＰＣ）Ｓ　島津製作所社製）のサンプルホルダーに固定し、ヒト血液を入り口側の面へマイクロピペット（エッペンドルフ社製）で５μｌ添加し、反対面の反射吸光度の反射吸光スペクトルを測定した。なお、血液の添加は孔径の小さい面から行った。血漿を添加した場合のスペクトルと比較し血色素の影響の有無を判定した。結果を表３に示す。

【００４１】測定条件

反射吸光スペクトル

測光値：反射率

波長範囲（ｎｍ）：開始７００　終了５００

スキャン速度：中速

スリット幅：２．０ｎｍ

サンプリングピッチ：１．０ｎｍ

【００４２】

【表３】

【表３】

	試験例１ しみ出し時間（sec）	試験例２ 血色素の影響
比較例１	４．６	有り
実施例１	５．２	無し
実施例２	５．７	無し
実施例３	６．８	無し
実施例４	７．３	無し
比較例２	１０．９	無し
比較例３	４．１	有り
実施例５	５．５	無し
実施例３	５．７	無し
実施例６	７．０	無し
比較例４	１０．２	無し
比較例５	しみ出さず	－
実施例７	７．１	無し
実施例３	５．７	無し
実施例８	５．４	無し
比較例６	－	－

【００４３】

【発明の効果】本発明の多孔質膜は、検体の展開速度が

速く、展開に要する時間を短くすることができるとともに、測色に際し、検体中の浮遊物を濾別・除去し、より高精度の測定を行うことができる。本発明の多孔質膜は、他の多孔質膜と積層することにより、検体の展開に要する時間を飛躍的に短縮することができ、かつ非常に測定精度が高い、検体中の特定成分測定用試験紙を提供することができる。

【００４４】特に、本発明の多孔質膜は、血液中の糖分を測定する血糖試験紙に有効に用いられることにより、血液の展開速度が速く、展開に要する時間を短くすることができるとともに、赤血球等の濾別物を十分に濾別・除去し、赤血球等の血色素の影響を排し、より高精度の測定を行うことができる。

【００４５】本発明の多孔質膜の製造方法は、検体の展開速度が速く、展開に要する時間を短くすることができるとともに、測色に際し、検体中の浮遊物を濾別・除去し、より高精度の測定を行うことができる多孔質膜の製造方法することができる。本発明の製造方法により得られた多孔質膜は、他の多孔質膜と積層することにより、検体の展開に要する時間を飛躍的に短縮することができ、かつ非常に測定精度が高い、検体中の特定成分測定用試験紙を提供することができる。

【００４６】特に、本発明の製造方法により得られた多孔質膜は、血液中の糖分を測定する血糖試験紙に有効に用いられることにより、血液の展開速度が速く、展開に要する時間を短くすることができるとともに、赤血球等の濾別物を十分に濾別・除去し、赤血球等の血色素の影響を排し、より高精度の測定を行うことができる。

フロントページの続き

Ｆターム(参考)　2G042 AA01 BD06 BD12 BD16 CA10
CB03 DA08 FA11 FB07 FC03
GA04 HA08
2G045 AA01 AA13 BA01 BA11 BB06
CA26
4F074 AA37 AA64 CB31 DA44
4J002 BJ001 CN032 GD05